

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-11 (Canceled)

12. (Currently Amended) A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a mutant yeast strain with sphingosine in the absence and presence of a candidate agent under conditions and for a time sufficient to observe in said mutant yeast strain an altered level of either (i) at least one sphingolipid intermediate, or (ii) activity of at least one component of a sphingolipid pathway, wherein:

the mutant yeast strain comprises a null allele of ~~at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, wherein said at least one gene comprises a~~ dihydrosphingosine-1-phosphate lyase 1 (DPL1) gene and a long chain base kinase 4 (LCB4) gene and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous sphingosine kinase (SK), wherein the nonendogenous SK comprises the amino acid sequence set forth in any one of SEQ ID NOs:19, 20, 21, 28 or 29, or a variant thereof having an amino acid sequence with at least 95% identity to the amino acid sequence of the nonendogenous SK, wherein the variant retains SK enzymatic activity, and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine; and

(b) comparing the level of either (i) or (ii) in the mutant yeast strain cultured in the presence of the candidate agent to the level of either (i) or (ii) in the mutant yeast strain cultured in the absence of the candidate agent, wherein an altered level in the presence of the agent indicates the agent modulates sphingolipid metabolism.

13. (Previously Presented) The method of claim 12 wherein said altered level of said at least one sphingolipid intermediate comprises a decrease in sphingosine-1-phosphate (S-1-P).

14. (Previously Presented) The method of claim 13 wherein said altered level of said activity of at least one component of a sphingolipid pathway comprises a decrease in the activity of said at least one nonendogenous SK.

15. (Canceled)

16. (Currently Amended) A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a null mutant yeast strain with sphingosine in the absence and presence of a candidate agent under conditions and for a time sufficient to observe altered growth of said mutant yeast strain, wherein:

the mutant yeast strain comprises a null allele of ~~at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, wherein said at least one gene comprises a DPL1 gene and a LCB4 gene and wherein said mutant strain of yeast has been genetically altered to~~ express at least one nonendogenous SK, wherein the nonendogenous SK comprises the amino acid sequence set forth in any one of SEQ ID NOs:19, 20, 21, 28 or 29, or a variant thereof having an amino acid sequence with at least 95% identity to the amino acid sequence of the nonendogenous SK, wherein the variant retains SK enzymatic activity, and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine; and

(b) comparing growth of the mutant yeast strain in the presence of the candidate agent to growth of the mutant yeast strain in the absence of the candidate agent, wherein an increase in growth of said mutant yeast strain in the presence of the candidate agent indicates the agent modulates sphingolipid metabolism.

17.-18 (Canceled)

19. (Currently Amended) The method of claim 16 wherein said at least one nonendogenous SK comprises human sphingosine kinase 1 (SPHK1) as set forth in SEQ ID NO:21, or a variant thereof having an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:21 and wherein the variant retains SK enzymatic activity.

20. (Currently Amended) A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a mutant yeast strain with an inducer in the absence and presence of a candidate agent under conditions and for a time sufficient to observe in said mutant yeast strain an altered level of either (i) at least one sphingolipid intermediate, or (ii) activity of at least one component of a sphingolipid pathway, wherein:

~~the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, wherein said at least one gene comprises a DPL1 gene and a LCB4 gene and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous SK under the control of a promoter that is induced by the inducer, wherein the nonendogenous SK comprises the amino acid sequence set forth in any one of SEQ ID NOs:19, 20, 21, 28 or 29, or a variant thereof having an amino acid sequence with at least 95% identity to the amino acid sequence of the nonendogenous SK, wherein the variant retains SK enzymatic activity, and wherein the mutant yeast strain exhibits growth inhibition in the presence of the inducer; and~~

(b) comparing the level of either (i) or (ii) in the mutant yeast strain cultured in the presence of the candidate agent to the level of either (i) or (ii) in the mutant yeast strain cultured in the absence of the candidate agent, wherein an altered level in the presence of the agent indicates the agent modulates sphingolipid metabolism.

21. (Previously Presented) The method of claim 20 wherein said altered level of said at least one sphingolipid intermediate comprises a decrease in phosphorylated long chain bases (LCBPs).

22. (Previously Presented) The method of claim 20 wherein said altered level of said activity of at least one component of a sphingolipid pathway comprises a decrease in the activity of said at least one nonendogenous SK.

23. (Currently Amended) The method of claim 22 wherein said at least one nonendogenous SK comprises human SPHK1 as set forth in SEQ ID NO:21, or a variant thereof having an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:21 and wherein the variant retains SK enzymatic activity.

24.-25 (Canceled)

26. (Currently Amended) The method of claim 20 wherein the mutant yeast strain further comprises a null allele of said at least one gene further comprises yeast sphingosine resistance 2 (YSR2).

27. (Currently Amended) A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a null mutant yeast strain with an inducer in the absence and presence of a candidate agent under conditions and for a time sufficient to observe altered growth of said mutant yeast strain, wherein:

the mutant yeast strain comprises a null allele of ~~at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, wherein said at least one gene comprises a DPL1 gene and a LCB4 gene and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous SK under the control of a promoter that is induced by the~~

inducer, wherein the nonendogenous SK comprises the amino acid sequence set forth in any one of SEQ ID NOs:19, 20, 21, 28 or 29, or a variant thereof having an amino acid sequence with at least 95% identity to the amino acid sequence of the nonendogenous SK, wherein the variant retains SK enzymatic activity, and wherein the mutant yeast strain exhibits growth inhibition in the presence of the inducer; and

(b) comparing growth of the mutant yeast strain in the presence of the candidate agent to growth of the mutant yeast strain in the absence of the candidate agent, wherein an increase in growth of said mutant yeast strain in the presence of the candidate agent indicates the agent modulates sphingolipid metabolism.

28.-29 (Canceled)

30. (Currently Amended) The method of claim 27 wherein the mutant yeast strain further comprises a null allele of said at least one gene further comprises YSR2.

31. (Currently Amended) The method of claim 30 wherein said at least one nonendogenous SK comprises human SPHK1 as set forth in SEQ ID NO:21, or a variant thereof having an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:21 and wherein the variant retains SK enzymatic activity.